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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,320	05/14/2001	Robert Bayer	040853-01-5108US	1113

43850 7590 02/09/2009

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EXAMINER	
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ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
02/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/855,320	BAYER, ROBERT	
	Examiner	Art Unit	
	GANAPATHIRAMA RAGHU	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *107-119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *107-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Application Status

In response to the Non-Final Office Action mailed on 06/09/08, applicant's response and amendment to specification on 11/07/08 is acknowledged. Said response, added new claims 109-119. Thus, claims 107-119 are pending in the application and are now under consideration for examination.

Objections and rejections not reiterated from previous action are hereby withdrawn.

Maintained-/Objection to Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. The specification contains hyperlinks to various site domains, for example on page 26. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. Appropriate correction is required.

Applicant has responded to this objection with the arguments that applicant has deleted reference to hyperlinks and have submitted a new specification amendment on 11/07/08.

Reply: Perusal of said amendment indicates that the applicants have submitted a clean copy without any mark-up or strike-through to show what subject matter has been deleted from the previous amendment and therefore the new specification amendment is not being considered and the objection is maintained. Examiner finds support for his position in the following section of the MPEP.

B. Amendments to the Specification

Amendments to the specification, other than the claims, computer listings (37 CFR 1.96) and sequence listings (37 CFR 1.825), must be made by adding, deleting or replacing a paragraph, by replacing a section, or by a substitute specification. In

order to delete, replace or add a paragraph to the specification of an application, the amendment must unambiguously identify the paragraph to be modified either by paragraph number (see MPEP § 608.01), page and line, or any other unambiguous method and be accompanied by any replacement or new paragraph(s). Replacement paragraphs must include markings to show the changes. A separate clean version of any replacement paragraphs is not required. Any new paragraphs must be presented in clean form without any markings (i.e., underlining).

Where paragraph numbering has been included in an application as provided in 37 CFR1.52(b)(6), applicants can easily refer to a specific paragraph by number when presenting an amendment. If a numbered paragraph is to be replaced by a single paragraph, the added replacement paragraph should be numbered with the same number of the paragraph being replaced. Where more than one paragraph is to replace a single original paragraph, the added paragraphs should be numbered using the number of the original paragraph for the first replacement paragraph, followed by increasing decimal numbers for the second and subsequent added paragraphs, e.g., original paragraph [0071] has been replaced with paragraphs [0071], [0071.1], and [0071.2]. If a numbered paragraph is deleted, the numbering of the subsequent paragraphs should remain unchanged. 37 CFR 1.121(b)(1)(ii) requires that the full text of any replacement paragraph be provided with markings to show all the changes relative to the previous version of the paragraph. The text of any added subject matter must be shown by underlining the added text. The text of any deleted subject matter must be shown by strike-through except that double brackets placed before and after the deleted characters may be used to show the deletion of five or fewer consecutive characters (e.g., [[error]]). The term "brackets" set forth in 37 CFR 1.121 means square brackets – [ ], and not parentheses – ( ). The text of any deleted subject matter must be shown by being placed within double brackets if strike-through cannot be easily perceived (e.g., deletion of the number "4" must be shown as [[4]]). As an alternative to using double brackets, however, extra portions of text may be included before and after text being deleted, all in strike-through, followed by including and underlining the extra text with the desired change (e.g., ~~number 4 as number14 as~~). For added paragraphs, 37 CFR 1.121(b)(*>1<)(iii) requires that the full text of any added paragraph(s) be presented in clean form without any underlining. Similarly, under 37 CFR 1.121(b)(*>1<)(iv), a marked up version does not have to be supplied for any deleted paragraph(s). It is sufficient to merely indicate or identify any paragraph that has been deleted. The instruction to delete may identify a paragraph by its paragraph number, page and line number, or include a few words from the beginning, and end, or the paragraph, if needed for paragraph identification.

Maintained-New-Matter/Objection to Specification

The amendment filed on 01/18/2008 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: page 26, lines 1-29 specification filed on 01/18/2008 are new matter. Support has not been provided for the newly added subject matter and no support is found in page 26, lines 9-10 as suggested by the applicant in the response dated 01/18/08. The scope of nucleic acid sequences; SEQ D NO: 1 and SEQ ID NO; 2 as claimed were not contemplated in the specification as originally filed dated 05/14/2001.

Applicant is required to cancel the new matter in the reply to this Office Action.

Applicant has responded to this objection with the arguments that:

1) In support of this amendment applicant pointed to page 24, lines 9-10 and

page 46, lines 22-23. However, the citation to page 24 was in error. Applicant intended to refer to page 26, lines 9-10.

2) page 26, lines 9-10, recites: "...and the βGal(1→4)βGlcNAc α1→3)fucosyltransferase (FucT-IV, FucT-V, FucT-VI and FucT-VIII, E.C.No.2.4.1.65) which are found in human serum.". This is the support for the sequences of the fucosyltransferase. Moreover, the incorporation by reference is found at page 46, lines 22-23. As such, applicants submit that neither the claims nor specification include New Matter.

Reply: 1) Applicant's admission on record of their error is acknowledged. However, applicant's instant response continues to have factual error in the arguments in that, the response filed on 01/18/08 and 04/08/08 did not allude to page 46, lines 22-23 at all. The only guidance that was given to the examiner in the response filed on 01/18/08 and 04/08/08 was the erroneous page number and lines i.e., page 24, lines 9-10.

Reply: 2) Perusal of the original specification, page 26 lines 9-10 indicates the following; examiner has copied the line 5-10 from the original specification filed on 05/14/2001.

Suitable fucosyltransferases for this reaction include the known Galβ(1→3,4)GlcNAcα(1→3,4) fucosyltransferase (FucT-III E.C. No. 2.4.1.65) which is obtained from human milk *(see, e.g.,* Palcic *et al., Carbohydrate Res.* 190:1-11 (1989); Prieels, *et al., J. Biol. Chem.*256:10456-10463 (1981); and Nunez, *et al., Can. J. Chem.* 59:2086-2095 (1981)) and the β(1→3,4)GlcNAcα(1→3,4) fucosyltransferases (FucT-IV, FucT-V, FucT-VI, and FucT- VII, E.C. No. 2.4.1.65) which are found in human serum.

At the outset for the record, examiner would like to state that the applicant's response does not clearly identify the subject matter which is incorporated and where it

is to be found and clearly point to which "specific portion" of the reference document where subject matter being incorporated can be found to "uniquely identify" the claimed sequence, per 37 CFR 1.57 (g)(2).

Even the three cited references do not refer to the incorporated sequence:

1. Palcic *et al., Carbohydrate Res.* 190:1-11 (1989) is directed to enzymic synthesis of oligosaccharides…wherein said enzyme with fucosyltransferase activity was purified by biochemical methods from milk and does not refer to the amino acid sequence of said enzyme either explicitly or implicitly.

2. Prieels, *et al., J. Biol. Chem.*256:10456-10463 (1981) is directed to co-purification of fucosyltransferases from milk by biochemical methods and does not refer to the amino acid sequence of said enzyme either explicitly or implicitly.

3. Nunez, *et al., Can. J. Chem.* 59:2086-2095 (1981)) is directed to synthesis of α- and β-L-fucopyranosyl phosphates and GDP fucose by sequential chemical synthesis method.

In the light of the above, examiner is unable to find clear support for the incorporated sequences either in the specification or in the cited sections of the specification or in the references of the cited section of the specification, based on the guidance provided by the applicants response. Therefore, examiner continues to maintain the objection.

New-Claim Rejections: 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 119 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 19 recites the phrase "... at least about 2 mg/ml", the metes and bounds of the phrase is not clear. The recitation of terms "at least" and "about" are inconsistent with each other and makes it unclear whether there is a discrete lower limit to said weight percent (see *Amgen Inc. v. Chugai pharmaceutical Co.,* F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991). Examiner suggests amending the phrase to "... at least 2 mg/ml" Clarification and correction is required.

Maintained-New Matter-Claim Rejections 35 USC § 112

Claims 107 and 108 and new claims 109-119 depending therefrom are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 107 and 108 and new claims 109-119 depending therefrom are rejected because the phrase (subject matter) "SEQ ID NO: 1 and SEQ ID NO: 2" is new matter. The scope of amino acid sequences as claimed was not contemplated in the specification as originally filed as said sequences were never incorporated by reference in the originally filed specification dated 05/14/2001 and examiner is unable to find support even in the guidance provided by instant applicants' response.

Applicants have responded to this rejection with the arguments that:

As noted above, applicant submits that the amendment of the specification and claims in the response to Final Office Action of January 18, 2008 did not contain New Matter because the sequences in question were incorporated by reference. The proper support for the amendment is set forth above.

Reply: As answered by the examiner above, there is no clear guidance provided by the applicant that has enabled the examiner to identify "specific portions" of the reference document or "uniquely identify" and where the subject matter being incorporated may be found in the cited references.

The attempt to incorporate subject matter into this application by reference to Palcic *et al., Carbohydrate Res.* 190:1-11 (1989), Prieels, *et al., J. Biol. Chem.*256:10456-10463 (1981) and Nunez, *et al., Can. J. Chem.* 59:2086-2095 (1981)), is ineffective because said documents do not teach the disclosed sequence either implicitly or explicitly or the applicant's response constitutes "specific portions" of the reference document or "uniquely identify" and where the subject matter being incorporated may be found in the cited references.

In addition, applicant is also directed to the following:

"An incorporating statement clearly identifying the subject matter which is incorporated and where it is to be found". *In re de Seversky, 474 F.2d 671, 177 USPQ 144 (CCPA 1973).*

"To incorporate material by reference, the host document must identify with detailed particularity what specific material it incorporates and clearly indicate where that material is found in the various documents." *Advanced Display Systems, Inc. v.*

Kent State Univ., 21 F.3d 1272, 54 USPQ2d 1673 (Fed.Cir.2000).

The incorporation by reference will not be effective until correction is made to comply with 37 CFR 1.57(b), (c), or (d). If the incorporated material is relied upon to meet any outstanding objection, rejection, or other requirement imposed by the Office, the correction must be made within any time period set by the Office for responding to the objection, rejection, or other requirement for the incorporation to be effective. Compliance will not be held in abeyance with respect to responding to the objection, rejection, or other requirement for the incorporation to be effective. In no case may the correction be made later than the close of prosecution as defined in 37 CFR 1.114(b), or abandonment of the application, whichever occurs earlier.

Any correction inserting material by amendment that was previously incorporated by reference must be accompanied by a statement that the material being inserted is the material incorporated by reference and the amendment contains no new matter. 37 CFR 1.57(f).

Maintained-Claim Rejections 35 USC § 102

Amendment to claim 107 has necessitated a new rejection.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 107, 109, 110 and 113-118 are rejected under 35 U.S.C. 102(b) as being anticipated by Lowe JB[1] (U.S. Patent No.: 5,324,663, date of patent 06/28/94) or Lowe[2]

et al., (U.S. Patent No.: 5,770,420, date of patent 06/23/98) when given the broadest reasonable interpretation.

Claims 107, 109, 110 and 113-118 are directed to a method for modifying the fucosylation pattern of a recombinant polypeptide comprising an acceptor moiety (Galβ1, 4GlcNAc-OR or NeuAcα2, 3Galβ1, 4GlcNAc-OR, wherein R is an amino acid, a saccharide, an oligosaccharide or an aglycon group), said method comprising a reaction mixture that comprises a fucose donor moiety, eukaryotic fucosyltransferase to achieve substantially uniform fucosylation pattern and said eukaryotic fucosyltransferase is recombinantly produced FucT-VI of SEQ D NO: 1 or FucT-VII of SEQ ID NO: 2 and wherein said eukaryotic fucosyltransferase lacks a membrane anchoring domain.

Lowe JB[1] disclose an isolated polypeptide (SEQ ID NO: 14) annotated as FucT-VI having 100% sequence homology to SEQ ID NO: 1 of the instant application and lacking a membrane anchoring domain and a method for modifying the fucosylation pattern of a recombinant polypeptide as claimed (entire document; especially column 2, lines 25-35; donor moieties, columns 8-10; use of said glycosyltransferase in enzymatic reactions to produce glycoproteins, glycolipids, oligosaccharides or polysaccharides of interest, column 13; recombinantly produced glycosyltransferase and abundant quantities of purified glycosyltransferase and use of said enzyme in solutions or solid matrix as bioreactors capable of enzymatic synthesis of glycoproteins column 16, lines 5-11; especially fucosyltransferase lacking membrane anchoring domain, columns 19-20; mechanisms for producing purified enzyme by the use of antibody affinity columns or fusion proteins comprising *Staph. aureus* protein A, columns 26-27 and column 46;

Example VI cloning, expression of SEQ ID NO: 14 including polypeptide lacking the membrane anchoring domain, purification of expressed enzyme to high purity using affinity columns and fucosyltransferase assays, columns 87-92).

Lowe[2] et al., disclose an isolated polypeptide (SEQ ID NO: 14) annotated as FucT-VI having 100% sequence homology to SEQ ID NO: 1 of the instant application and lacking a membrane anchoring domain and a method for modifying the fucosylation pattern of a recombinant polypeptide as claimed (entire document; especially column 2, lines 25-35; donor moieties, columns 10-12; use of said glycosyltransferase in enzymatic reactions to produce glycoproteins, glycolipids, oligosaccharides or polysaccharides of interest, column 14; recombinantly produced glycosyltransferase and abundant quantities of purified glycosyltransferase and use of said enzyme in solutions or solid matrix as bioreactors capable of enzymatic synthesis of glycoproteins column 13; especially fucosyltransferase lacking membrane anchoring domain, column 21; Example VI cloning, expression of SEQ ID NO: 14 including polypeptide lacking the membrane anchoring domain, purification of expressed enzyme to high purity using affinity columns and fucosyltransferase assays, mechanisms for producing purified enzyme by the use of antibody affinity columns or fusion proteins comprising *Staph. aureus* protein A, columns 87-93).

Therefore the references of Lowe JB[1] (U.S. Patent No.: 5,324,663, date of patent 06/28/94) or Lowe[2] et al., (U.S. Patent No.: 5,770,420, date of patent 06/23/98) is deemed to anticipate claims 107, 109, 110 and 113-118 as written (also see provided sequence alignments).

Applicant has traversed the above rejection with the following arguments:

1) 5,324,663 fails to disclose the transfer of fucose to any recombinant polypeptide…This is not, however, a description of an *in vitro* reaction as claimed. Examiner has not pointed out any recitation in the 5,324,663 that discloses an enzymatic reaction as claimed, wherein the glycopeptide has a substantially uniform glycosylation.

Reply 1): Contrary to applicant's arguments 5,324,663 teaches both *in vitro* and *in vivo* fucosylation of glycoproteins of interest as indicated by the title of the document " Methods and products for the synthesis of oligosaccharide structures on glycoproteins, glycolipids, or as free molecules…. furthermore, applicants are directed to the following sections of 5,324,663 document.

Column 2: lines 56-60 discloses; "It is another object of this invention to provide these unmodified and modified isolated genes and cDNAs, and to use them, for example in modifying cell surface oligosaccharide structure via gene transfer approaches or via in vitro glycosylation reactions."

Column 8: lines 15-68 discloses; fucosyltransferases, another type of glycosyltransferases are provided by the present invention, are associated with the following linkages: (1) …. Including the linkages (Galβ1, 4GlcNAc-OR or NeuAcα2, 3Galβ1, 4GlcNAc-OR, wherein R is an amino acid, a saccharide, an oligosaccharide or an aglycon group).

Column 10: lines 45-61 discloses; "In another embodiment...The enzyme of the invention transforms the precursor into desired oligosaccharide, polysaccharide, glycolipid, or glycoprotein which is thereby obtained".

Column 13: lines 43-45 discloses; "in another embodiment…These enzymes can be used in bioreactors in *in vitro*, large scale, synthesis of oligosaccharides or glycolipids or for glycosidic modification of proteins and glycoproteins".

Column 16: lines 30-33 discloses; "enzyamtic catalysis is extraordinarily efficient; virtually complete conversion of substrate to product can be achieved. By contrast, chemical synthesis of these structures is a multi-step process; yields at each step may be much less than 100%...".

2) Likewise 5,770,420 fails to disclose the transfer of fucose to any recombinant polypeptide…This is not, however, a description of an *in vitro* reaction as claimed. Examiner not pointed out any recitation in the 5,324,663 that discloses an enzymatic reaction as claimed, wherein the 5,770,420 has a substantially uniform glycosylation.

Reply 2): Contrary to applicant's arguments 5,770,420 teaches both *in vitro* and *in vivo* fucosylation of glycoproteins of interest as indicated by the title of the document " Methods and products for the synthesis of oligosaccharide structures on glycoproteins, glycolipids, or as free molecules…. furthermore, applicants are directed to the following sections of 5,770,420 document.

Column 2: lines 46-50 discloses; "It is another object of this invention to provide these unmodified and modified isolated genes and cDNAs, and to use them, for

example in modifying cell surface oligosaccharide structure via gene transfer approaches or via in vitro glycosylation reactions."

Columns 9-10: lines 1-68 discloses; fucosyltransferases, another type of glycosyltransferases are provided by the present invention, are associated with the following linkages: (1) …. Including the linkages (Galβ1, 4GlcNAc-OR or NeuAcα2, 3Galβ1, 4GlcNAc-OR, wherein R is an amino acid, a saccharide, an oligosaccharide or an aglycon group).

Columns 13-14: lines 65-68 of column 13 and lines 1-10 of column 14 discloses; "in another embodiment…These enzymes can be used in bioreactors in *in vitro*, large scale, synthesis of oligosaccharides or glycolipids or for glycosidic modification of proteins and glycoproteins".

Column 15: lines 33-35 discloses; "in another embodiment…These enzymes can be used in bioreactors in *in vitro*, large scale, synthesis of oligosaccharides or glycolipids or for glycosidic modification of proteins and glycoproteins".

Column 18: lines 32-36 discloses; " enzyamtic catalysis is extraordinarily efficient; virtually complete conversion of substrate to product can be achieved. By contrast, chemical synthesis of these structures is a multi-step process; yields at each step may be much less than 100%...".

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 107, 109, 110 and 113-118 are rejected under 35 U.S.C. 102(e) as being anticipated by Lowe JB[3] (U.S. Patent No.: 6,268,193, date of patent 07/31/01) or Sasaki

et al., (U.S. Patent No.: 7,094,530, date of patent 08/22/06, claiming priority to US Application No.: 08/361,306 filed on 11/29/1994), when given the broadest reasonable interpretation.

Claims 107, 109, 110 and 113-118 are directed to a method for modifying the fucosylation pattern of a recombinant polypeptide comprising an acceptor moiety (Galβ1, 4GlcNAc-OR or NeuAcα2, 3Galβ1, 4GlcNAc-OR, wherein R is an amino acid, a saccharide, an oligosaccharide or an aglycon group), said method comprising a reaction mixture that comprises a fucose donor moiety, eukaryotic fucosyltransferase to achieve substantially uniform fucosylation pattern and said eukaryotic fucosyltransferase is recombinantly produced FucT-VI of SEQ D NO: 1 or FucT-VII of SEQ ID NO: 2 and wherein said eukaryotic fucosyltransferase lacks a membrane anchoring domain.

Lowe JB[3] disclose an isolated polypeptide (SEQ ID NO: 14) annotated as FucT-VI having 100% sequence homology to SEQ ID NO: 1 of the instant application and lacking a membrane anchoring domain and a method for modifying the fucosylation pattern of a recombinant polypeptide as claimed (entire document; especially column 2, lines 25-35; donor moieties, columns 8-10; use of said glycosyltransferase in enzymatic reactions to produce glycoproteins, glycolipids, oligosaccharides or polysaccharides of interest, column 13; recombinantly produced glycosyltransferase and abundant quantities of purified glycosyltransferase and use of said enzyme in solutions or solid matrix as bioreactors capable of enzymatic synthesis of glycoproteins columns 13-15; especially fucosyltransferase lacking membrane anchoring domain, column 19; Example VI cloning, expression of SEQ ID NO: 14 including polypeptide lacking the

membrane anchoring domain, purification of expressed enzyme to high purity using affinity columns and fucosyltransferase assays, mechanisms for producing purified enzyme by the use of antibody affinity columns or fusion proteins comprising *Staph. aureus* protein A, columns 83-90; recombinantly purified fucosyltransferase isolated with grater than 95%-98% purity with very high specific activity; claims 1-10, columns 123-124).

Sasaki et al., disclose an isolated polypeptide (SEQ ID NO: 2) having 100% sequence homology to SEQ ID NO: 2 of the instant application and lacking a membrane anchoring domain and a method for modifying the fucosylation pattern of a recombinant polypeptide as claimed (entire document; especially column 9, lines 15-40; fucosyltransferase lacking membrane anchoring domain, column 27, lines 1-16, columns 45-46; column 34, lines 27-49; activity assays, columns 35-36; industrial applicability, column 54; claims, columns 73-74).

Therefore, Lowe JB[3] (U.S. Patent No.: 6,268,193, date of patent 07/31/01) or Sasaki et al., (U.S. Patent No.: 7,094,530, date of patent 08/22/06, claiming priority to US Application No.: 08/361,306 filed on 11/29/1994), disclosures are deemed to anticipate claims 107, 109, 110 and 113-118 of the instant invention (also see provided sequence alignments).

Applicant has traversed the above rejection with the following arguments:

3) 6,268,193 patent appears to contain the same disclosure as 5,324,663. As such, the response to the rejection based on 5,324,663 holds true for 6,268,193 as well.

Reply 3): Examiner is in agreement with the applicant's observation that 6,268,193 patent appears to contain the same disclosure as 5,324,663 and as such examiner' answer with regard to 5,324,663, 102 (b) rejections equally applies to the instant rejection based on 6,268,193 patent.

4) Applicant has found no disclosure in Sasaki et al., (U.S. Patent No.: 7,094,530) of an *in vitro* method to transfer fucose to a full-length recombinant glycopeptides.

Reply 4): Contrary to applicant's arguments 7,094,530 teaches both *in vitro* and *in vivo* fucosylation of glycoproteins of interest.

Applicants are directed to the following sections of 7,094,530 document.

Column 9: lines 8-25 discloses; "Alpha-1, 3-fucosyltransferase produced in accordance with the present invention can be purified using ordinary methods of purifying glycosyltransferases… or purify the same by affinity chromatography".

Column 9: lines 31-40 discloses; "Carbohydrate chains can be synthesized *in vitro* using Alpha-1, 3-fucosyltransferase of the present invention. For example, GlcNAC in lactosamine structure (Galβ1-4GlcNAc structure) in glycoproteins, glycolipids or oligosaccharides can be provided with α1→3 linkage".

Column 74: Claim 14 directed to an *in vitro* method of glycosylation.

Maintained-Claim Rejections 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 107-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowe JB[1] (U.S. Patent No.: 5,324,663, date of patent 06/28/94) or Lowe[2] et al., (U.S. Patent No.: 5,770,420, date of patent 06/23/98) or Lowe JB[3] (U.S. Patent No.: 6,268,193, date of patent 07/31/01) or Sasaki et al., (U.S. Patent No.: 7,094,530, date of patent 08/22/06, claiming priority to US Application No.: 08/361,306 filed on 11/29/1994).

Claims 107-119 are directed to a method for modifying the fucosylation pattern of a recombinant polypeptide comprising an acceptor moiety (Galβ1, 4GlcNAc-OR or NeuAcα2, 3Galβ1, 4GlcNAc-OR, wherein R is an amino acid, a saccharide, an oligosaccharide or an aglycon group), said method comprising a reaction mixture that comprises a fucose donor moiety, eukaryotic fucosyltransferase to achieve substantially uniform fucosylation pattern and said eukaryotic fucosyltransferase is recombinantly produced FucT-VI of SEQ D NO: 1 or FucT-VII of SEQ ID NO: 2 and wherein said eukaryotic fucosyltransferase lacks a membrane anchoring domain, wherein the concentration of said recombinant FucT-VI or FucT-VII fucosyltransferase is at least 1 Unit/ml ml (as in claim 108) or wherein said full-length recombinant glycopetide is a clotting factor or Factor VIII or Factor IX (as in claims 111 and 112) or at least about 2mg/ml (as in claim 119).

Lowe JB[1] or Lowe[2] et al., or Lowe JB[3] disclose an isolated polypeptide (SEQ ID NO: 14) annotated as FucT-VI having 100% sequence homology to SEQ ID NO: 1 of the instant application and lacking a membrane anchoring domain and to a method for modifying the fucosylation pattern of a recombinant polypeptide and highly purified

polypeptide (entire documents).

Similarly, Sasaki et al., disclose an isolated polypeptide (SEQ ID NO: 2) having 100% sequence homology to SEQ ID NO: 2 of the instant application and lacking a membrane anchoring domain and to a method for modifying the fucosylation pattern of a recombinant polypeptide and highly purified polypeptide (entire document) and as discussed above in 102 (b) and 102(e) rejections.

However, said references are silent regarding the concentration of said recombinant FucT-VI or FucT-VII fucosyltransferase is at least 1 Unit/ml (as in claim 108) or wherein said full-length recombinant glycopetide is a clotting factor or Factor VIII or Factor IX (as in claims 111 and 112) or at least about 2mg/ml (as in claim 119).

It would have been obvious to a person of ordinary skill in the art to combine the above teachings to reconstitute the expressed polypeptides in a buffer system to any required concentration such as 1 Unit/ml or at least about 2mg/ml for the assay of the enzymatic activity of FucT-VI or FucT-VII fucosyltransferase enzymes and the use of said enzymes in method for modifying the fucosylation pattern of any recombinant polypeptide such as clotting factor or Factor VIII or Factor IX. Said references teach the isolation and purification of FucT-VI or FucT-VII fucosyltransferase enzymes, said purity in the range of 95%-98%, the protein concentration of said enzymes such as ug/ul, enzyme assays, methods for glycosylation of products of interest and determining the efficiency of glycosylation by said enzymes in said glycosylated products. Therefore a skilled artisan based on the knowledge and information provided in said teachings will certainly be able to determine the specific concentration i.e., Units/ml of said purified

enzymes necessary for successfully fucosylating any recombinant polypeptide such as clotting factor or Factor VIII or Factor IX (modify the fucosylation pattern) and to reconstitute the purified enzymes in a suitable buffer to the requisite amount of activity. Motivation to combine the teachings derives from the fact that FucT-VI or FucT-VII fucosyltransferase enzymes are employed in industrial applications for their ability to synthesize various sugar molecules and modification of proteins or sugars by their ability to transfer sugar moieties on acceptor sites of peptide or sugar chain acceptors and furthermore said enzymes when provided with known activity information such as Units/ml will be useful for immediate use and applications without the additional step of determining the specific activity of said enzymes. The expectation of success is high, because, the disclosure of Lowe JB[1] or Lowe[2] et al., or Lowe JB[4] teach an isolated polypeptide (SEQ ID NO: 14) annotated as FucT-VI having 100% sequence homology to SEQ ID NO: 1 of the instant application and lacking a membrane anchoring domain, methods for modifying the fucosylation pattern of any recombinant polypeptide and highly purified polypeptide (entire documents) and similarly, Sasaki et al., disclose an isolated polypeptide (SEQ ID NO: 2) having 100% sequence homology to SEQ ID NO: 2 of the instant application methods for modifying the fucosylation pattern of a recombinant polypeptide and highly purified polypeptide (entire document).

Therefore, the above reference renders claims 107-119 *prima facie* obvious to one of ordinary skill in the art.

Applicants have traversed this rejection with the following arguments:

The alleged *prima facie* obviousness is deficient because the cited references alone, or in any combination, fail to teach each and every element found in the claims. In, particular, the combination of references fail to teach full-length recombinant glycopeptide as an *in vitro* substrate for fucosylation (pages 11-12 of applicants response dated 11/07/08).

Reply: These arguments are found unpersuasive, examiner has cited the relevant sections from each and every reference wherein all the elements of the instant invention are taught.

The basis for the examniner to continue to hold his position is reasoned below; examiner has provided unequivoical evidence for combining the cited references and that the cited references have been properly applied in this obviousness rejection in accordance with the factual enquires set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966) and the rationale for TSM test (Teaching, Suggestion and Motivation) according to KSR ruling. Furthermore the cited references teach all the limitations of the instant claims.

The cited references render claims 107-119 *prima facie* obvious to one of ordinary skill in the art when one applies the Teaching, Suggestion and Motivation (TSM) test under the rationale for arriving at a conclusion of obviousness as suggested by the KSR ruling. The rationale applied for this rejection is as follows:

(1) Combining prior art elements according to known method to yield predictable results.

(2) Simple substitution of one known element for another to obtain predictable results.

(3) "Obvious to try"- choosing from a finite number of identified, predictable solution, with a reasonable expectation of success.

The examiner has provided the rationale to support a conclusion that the claims would have been obvious in that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods **with no change in their respective functions**, and the combination yielded nothing more than predictable results to one of ordinary skill in the art. KSR, 550 U.S. at ___, 82 USPQ2d at 1395; Sakraida v. AG Pro, Inc., 425 U.S. 273, 282, 189 USPQ 449, 453 (1976); Anderson 's-Black Rock, Inc. v. Pavement Salvage Co., 396 U.S. 57, 62-63, 163 USPQ 673, 675 (1969); Great Atlantic & P. Tea Co. v. Supermarket Equipment Corp., 340 U.S. 147, 152, 87 USPQ 303, 306 (1950).

Summary of Pending Issues

The following is a summary of issues pending in the instant application.

1. Amended claims 107-119 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement/New-matter rejection.

2. Claims 107, 109, 110 and 113-118 are rejected under 35 U.S.C. 102(b) as being anticipated by Lowe JB[1] (U.S. Patent No.: 5,324,663, date of patent 06/28/94) or Lowe[2] et al., (U.S. Patent No.: 5,770,420, date of patent 06/23/98).

3. Claims 107, 109, 110 and 113-118 are rejected under 35 U.S.C. 102(e) as being anticipated by Lowe JB[3] (U.S. Patent No.: 6,268,193, date of patent 07/31/01) or

Sasaki et al., (U.S. Patent No.: 7,094,530, date of patent 08/22/06, claiming priority to US Application No.: 08/361,306 filed on 11/29/1994).

4. Claims 107-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowe JB[1] (U.S. Patent No.: 5,324,663, date of patent 06/28/94) or Lowe[2] et al., (U.S. Patent No.: 5,770,420, date of patent 06/23/98) or Lowe JB[3] (U.S. Patent No.: 6,268,193, date of patent 07/31/01) or Sasaki et al., (U.S. Patent No.: 7,094,530, date of patent 08/22/06, claiming priority to US Application No.: 08/361,306 filed on 11/29/1994).

Conclusion

None of the claims are allowable. Claims 107-119 are rejected for the reasons identified in the Rejections and Summary sections of this Office Action. Applicants must respond to the objections/rejections in each of the sections in this Office Action to be fully responsive for prosecution.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached between 8 am-4: 30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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